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## **Table of Contents**

Front Cover	1
Standard Form 298	2
Foreword	3
Table of Contents	4
Introduction	5
Body	6-8
Key Research Accomplishments	9
Reportable Outcomes	9
Conclusions	10
References	11
Appendices	12-13

## Introduction

This project provides a novel opportunity to measure preferences for key health outcomes in a well-characterized cohort of men with prostate cancer detected via prostate-specific antigen (PSA) and treated with radical prostatectomy between 1994 and 1997. This project is innovative in that no previous investigators have assessed preferences for outcomes in a large cohort of men who were actually experiencing the post-treatment outcomes of interest. Because we had recently evaluated urinary and sexual function and bother in this cohort,<sup>1</sup> we were able to stratify our cohort to target men for further study that had experienced a range of outcomes in these domains. More specifically, we systematically measured preferences for living with a health state in men who were experiencing problems with urinary and/or sexual functioning, and men who were not experiencing problems in these domain. Preliminary analysis indicate significant differences in preferences by outcome group. However, final conclusions are pending upon additional data. Ultimately, linking preferences for health states with current functioning will provide more accurate estimates of patient preferences for use in decision analysis models. These models are of critical importance because the proportion of men in the US being screened and treated for prostate cancer is increasing.<sup>2</sup> Although direct evidence from randomized controlled trials are likely to provide the most definitive estimate about the overall effectiveness of screening and treatment for prostate cancer, the results of such studies will not be available for many years. Decision makers - patients, physicians, and health policy makers - must act before these results are available. Supporting these decision makers requires a better understanding of how men feel about their quality of life after surgical management of their disease. These data will allow a more accurate evaluation of the immediate costs of screening in the absence of long-term data from randomized trials. Since the established risk factors for prostate cancer are nonmodifiable, screening is the only currently viable method for affecting prostate cancer morbidity and mortality; therefore, we need to know how screening and resultant treatment affect quality of life.

## Body

The following outlines the progress in the first 12 months of funding with regard to each task outlined in our originally submitted "Statement of Work."

### Task 1 "Development of computer-based health utility assessment module (months 1-6)"

Measures of health utilities are used to adjust estimates of life expectancy that are the endpoints of decision analysis models. Recently, interview and computer-based methods have been developed to measure health utilities in individual patients. These methods use techniques such as the standard reference gamble<sup>3</sup> or time trade-off<sup>4</sup> to elicit utilities. Using these methods, preferences are derived implicitly based on the individual's response to decision situations.<sup>5</sup> For example, in the time trade-off method an individual is presented with a paired comparison in which he or she must choose between two alternatives. In the case of a chronic health condition (i.e., incontinence following surgical treatment for prostate cancer), one alternative is to live with the chronic condition for the remainder of life, the second alternative is to have a shorter life, but to live in the absence of the chronic condition. The individual is asked to choose between these two alternatives, varying the length of the "shorter life" until the individual is indifferent between the two alternatives. The indifference point is the utility for the chronic condition. The less desirable the health condition, the greater the amount of life the individual will give up in order to be free of the chronic condition. In this instance, the chronic condition would have a low utility.

For the current project we have used the U-titer computer program<sup>6</sup> as the platform for building automated preference interviews. More specifically, we have successfully computerized both standard gamble and time trade-off methods for eliciting utilities for current health states in our patient groups. The final version of the interview was completed after testing preliminary programs with 25 pilot subjects (men with prostate cancer who were not eligible for the current study). To use the automated interview, the subject sits in front of the computer and answers a series of questions presented on the screen. The subject responds to questions using a track ball to select the appropriate answers. Overall, the computerized interview was well accepted by our subject population. The majority of subjects were able to complete the interview independently after a brief introduction by the research assistant.

The second task completed in the initial 6 months was the development of databases and quality control procedures for data management. More specifically, databases were created to link the computerized interview data with the questionnaire responses measuring current urinary and sexual functioning.

### Task 2 "Participant selection and data collection (months 7-18)."

Participants were recruited from our ongoing longitudinal study of outcomes in men with screen-detected prostate cancer (N=2,237).<sup>7</sup> Because these men were all originally enrolled in our PSA screening studies, we had extensive data regarding demographics, primary treatment,

and cancer stage and grade. In addition, we also had extensive information regarding quality-of-life outcomes after treatment.<sup>1</sup> We selected for further study only those men who had cancer detected between 1994 and 1997, had radical prostatectomy as their primary treatment, and had returned a prior questionnaire measuring quality of life (N=432). We selected this time frame so that outcomes would be more likely attributed to the treatment and not to aging per se; we selected only surgery patients because this treatment is being increasingly used in the US. Additionally, within this cohort of 432 men we *a priori* defined positive, intermediate, and negative health states based on previous self-reports of urinary and sexual functioning. We defined these health states based on prior responses to questions regarding the level of bother associated with current urinary function and level of bother associated with current sexual function. More specifically, we selected for further study men from three categories of outcomes: (1) men who were bothered by both their current sexual and urinary functioning, (2) men who were bothered by their current sexual functioning, but not urinary functioning, and (3) men who were not bothered by either their current sexual or urinary functioning. By sampling men from these outcome categories, we hoped to obtain utilities from equal numbers of men within each of these health states; however, we also reassessed their current urinary and sexual functioning to monitor potential drift between outcome categories.

To serve as our sampling frame, we randomly selected approximately 80 men from each of the three outcome categories defined above. Within these groups, we again randomly selected men until we had recruited ~50 men in each group that had completed the interview and the reassessment of function and bother. Refusal rates ranged from 12-16% across groups. Of the men who agreed to participate, we also randomly selected a subset of 30 men to complete the computerized interview twice at two-week intervals to assess test-retest reliability of the computerized interview. We found an interclass correlation coefficient (ICC) of 0.8 for the time trade-off method and an ICC of 0.7 for the standard gamble method for assessment of utilities. These values were within range of other computerized assessments of utilities<sup>8</sup> and indicated that the computerized measures had acceptable test-retest reliability.

Of the 155 men who completed the interview and the questionnaire, approximately 40% drifted from their original outcome group when recategorized based on current urinary and sexual function. This was especially problematic for the group originally bothered by both urinary and sexual function. More specifically, based on the questionnaire responses at the time of the utilities assessment, 58% of these men switched from their original group to either (1) having only bother associated with sexual function, or (2) not bothered by either sexual or urinary function. In the other two original study groups, only 30% of the men were recategorized based on current functioning. Overall, the utility for current health state was high when measured via either standard gamble or time trade-off (mean  $\pm$  sd = .90  $\pm$  .25 and .86  $\pm$  .27, respectively). An interim analysis including approximately 50% of the data showed no significant group differences in utilities. However, a recently updated analysis (including all the completed interviews), showed a significant difference in mean utilities assessed via standard gamble method when comparing the original groups (see Appendices, Table 1). Significant group differences for both the time trade-off and standard gamble utilities were also found when outcome groups were recategorized based

upon most recent functioning (see Appendices, Table 2). Therefore, these preliminary results indicate that men with greater bother associated with sexual and urinary functioning were willing to give up more life to be in perfect health. These results support our original hypothesis. However, we have concerns that the sample size for the recategorized group for bother associated with both sexual and urinary function is too small ( $N = 26$ ) to provide stable estimates of the mean utilities. At the time of the interim analysis we had written to the DOD to request an approval for additional subject recruitment to increase the power of our study. Although we now have achieved significant group differences, we would still prefer to recruit additional subjects to increase the number of subjects in the bother associated with both sexual and urinary functioning group (i.e., increase the sample size to  $\sim 50$  as proposed originally). We intend to use the same eligibility criteria for recruiting new participants, except to extend the cutoff for treatment from 1997 through 1998. This change in the study criteria should provide approximately 100 additional participants. Given that we have budgeted through month 18 for subject recruitment activities, and given that we have already met our original recruitment goals, we feel that it is likely that we will be able to achieve our new target sample sizes.

Task 3            “Statistical Analysis and write-up of results (months 19-24).”

The original statement of work intended for the last 6 months of funding to be devoted to statistical analysis and write-up of results. Although we are planning to collect more data pending DOD approval, we should still be on schedule to be ready for analysis by the last 6 months.



### **Key Research Accomplishments**

- (1) Development of computerized interview for assessment of preferences for health states in men with prostate cancer.
- (2) Achieved acceptable test-retest reliability for computerized interview.
- (3) Achieved original participant recruitment goals.
- (4) Performed preliminary data analysis showing significant differences in outcome groups with regard to preferences for current health states.

### **Reportable Outcomes**

- (1) Development of a reliable computerized interview for assessment of preferences for health states in men with prostate cancer.
- (2) Development of a database with preferences for health states linked to objective measures of quality of life and clinical data.

## **Conclusions**

In the first 12 months of funding we have made good progress in that we have already completed our participant recruitment goals. However, we hope to collect more data so that we will meet our original recruitment goals for each outcome group given the shifts in our outcomes groups. Preliminary analysis indicated significantly lower utilities for men bothered by both their current sexual and urinary functioning. However, the overall mean utilities were high (ranging from .86 to .90), indicating that men who have undergone surgical management of prostate cancer are not willing to trade-off much to be in perfect health. This indicates that the quantification of quality-of-life outcomes may need to be reevaluated in decision analysis models. Measurement of patient preferences for health states following prostate surgery has never been performed in a large sample of men who were actually experiencing the outcomes of interest. In addition, the current study provides a link between utilities for health following surgical management of prostate cancer and more widely used measure of functional status and bother. Such a linkage will be of increased importance as outcomes studies employing these measures are used as the basis for decision analysis and cost-effectiveness analysis.

## References

1. Carvalhal GF, Smith DS, Ramos C, Krygiel J, Mager DE, Yan Y. Correlates of dissatisfaction with treatment in patients with prostate cancer diagnosed through screening. *J Urol* (in press).
2. Jacobson SJ, Katusic SK, Bergstralh EJ, Oesterling JE, Ohrt D, Klee GG, Chute CG, Lieber MM. Incidence of prostate cancer diagnosis in the eras before and after serum prostate-specific antigen testing. *JAMA* 1995;274:1445.
3. Von Neumann J, Morgenstern O. *Theory of Games and Economic Behavior* (3<sup>rd</sup> Edition). New York: Wiley & Sons, 1953.
4. Torrance GW, Thomas WH, Sackett DL. A utility maximization model for evaluation of health care programs. *Health Serv Res* 1972;7:118.
5. Torrance GW. Utility approach to measuring health-related quality of life. *J Chron Dis* 1987;40:593.
6. Sumner W, Nease RF Jr, Littenberg B, Kneeland T, O'Connor G. U-titer. A utility assessment tool. *Med Decis Making* 1991;11:327.
7. Smith DS, Catalona WJ, Herschman JD. Longitudinal screening for prostate cancer with prostate specific antigen. *JAMA* 1996;276:1309.
8. Nease RF Jr, Kneeland T, O'Connor G. Variation in patient utilities for outcomes of the management of chronic stable angina. Implications for clinical practice guidelines. *JAMA* 1995;273:1185.

## Appendices

Table 1

Mean and Median Time-Trade Off and Standard Gamble Utilities, Stratified by Original Outcome Group

Outcome Group:	Bothered by Urinary and Sexual Functioning (N =55)	Bothered by Sexual Functioning (N=50)	Bothered by Neither (N=50)	P*
Time-Trade Off Method				
Mean (+SD)	.81 ( $\pm$ .31)	.90 ( $\pm$ .20)	.88 ( $\pm$ .28)	0.3
Median	.92	.94	.99	
Standard Gamble Method				
Mean (+SD)	.83 ( $\pm$ .31)	.96 ( $\pm$ .11)	.93 ( $\pm$ .26)	.002
Median	.94	.99	.99	

\* = P values represent results for Kruskal-Wallis test.

Table 2

Mean and Median Time-Trade Off and Standard Gamble Utilities, Stratified by Recategorized\* Outcome Groups

Outcome Group:	Bothered by Urinary and Sexual Functioning (N =26)	Bothered by Sexual Functioning (N=62)	Bothered by Neither (N=57)	P**
Time-Trade Off Method				
Mean (+SD)	.74 (± .37)	.85 (± .24)	.92 (± .25)	0.001
Median	.82	.92	.99	
Standard Gamble Method				
Mean (+SD)	.79 (± .35)	.89 (± .25)	.96 (± .21)	.0001
Median	.91	.98	.99	

\* = Outcome groups were recategorized based on reassessment of bother associated with sexual and urinary function at the time of the computerized interview. Ten (10) men were excluded from the analysis because their original outcome group shifted from "bothered by both urinary and sexual function", or "bothered by sexual function only", to "bothered by urinary function only." The latter outcome group was not included in our original study in that proportionately very few men were bothered only by urinary functioning.

\*\* = P values represent results for Kruskal-Wallis test.